UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,118	02/25/2002	Didier Lefevre	20198/0059	8544

7590 06/01/2005

George R. Pettit
Connolly Bove Lodge & Hutz LLP
Suite 800
1990 M Street, N.W.
Washington, DC 20036-3425

EXAMINER	
GABEL, GAILENE	
ART UNIT	**PAPER NUMBER**
1641	

DATE MAILED: 06/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,118	LEFEVRE ET AL.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 March 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *12-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-19* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/25/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's amendment and arguments, filed on March 22, 2005, is acknowledged. Claims 1-11 have been amended. Claim 19 has been added. Claims 12-18 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Accordingly, claims 1-19 are pending and claims 1-11 and 19 are under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, (part 2) lacks antecedent support in reciting, "the intracellular nucleic acids".

Claim 2 is unclear in reciting, "wherein the sample is of blood". Perhaps, Applicant intends, "wherein the sample is blood".

Claim 5 is vague and indefinite in failing to recite a positive limitation in reciting, "capable of combining". Further, it is unclear what Applicant intends to encompass in using the term "combining" since it appears to mean "mixing with intracellular

ribonucleic acid". Perhaps, Applicant intends that "the stain is capable of binding to intracellular ribonucleic acid to thus enhance a fluorescent signal from the stain". Additionally, it is unclear how a "stain is enhanced", i.e. an amount of stain can be increased so as to effectively enhance a signal therefrom.

Claim 6 is redundant and is therefore, indefinite in reciting, "wherein the stain is selected from the group selected from".

Claim 7 is vague and indefinite because it implies but fails to specifically define that the cell membrane in the instant claim refers to those from the unlysed cells. Perhaps, Applicant intends "capable of increasing permeability of cell membrane in unlysed cells; hence, promoting the penetration of stain into the unlysed cells.

Claim 8 lacks clear antecedent support in reciting, "the agent promoting membrane penetration". Perhaps, Applicant intends, "the at least one membrane penetration agent" which refers back to the same element in claim 7.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

3. Claims 1-11 stand rejected under 35 U.S.C. 102(b) as being anticipated by Sakata (US 5,496,734) for reasons of record.

Sakata discloses a reagent for identifying, counting, and classifying blood cells. The reagent comprises a lysing agent or cationic detergent (surfactant) such as quaternary ammonium salts at a concentration that lyses erythrocytes and a fluorescent stain (labeling substance) that can permeate through permeabilized cell membrane of nucleated unlysed cells (leucocytes) so as to incorporate with and label intracellular nucleic acids of the unlysed nucleated cells (see column 6, line 64 to column 7, lines 1-67, column 8, lines 1-12, and especially column 10, lines 44-62). According to Sakata, nonionic surfactant may also be added to the reagent to control the effects of the ionic surfactant toward cell membrane (see column 9, line 14 to column 10, line 4). Sakata provides that the surfactant may function by removing part of substances which constitute cell membrane, i.e. ionophore; thus yielding pores in the cell membrane to allow passage of substances such as stain into the cell (see column 10, line 63 to column 11, line 8). Stains used with the reagent include Thiazole Orange, Acridine Orange, ethidium bromide, and propidium bromide (see column 8, lines 18-29). Sakata teaches that alcohol can be added as fixing agent to minimize loss of cytoplasms and granules and to optimize degree of damage of the cell membranes. According to Sakata, formaldehyde and gluteraldehyde are also used as fixing agents (see column 10, lines 10-39 and column 2, lines 13-19). The reagent further includes anticoagulant and buffer (see column 8, line 64 to column 9, line 13).

4. Claims 1-7 and 9-11 stand rejected under 35 U.S.C. 102(e) as being anticipated by Deka et al. (US 6,271,035) for reasons of record.

Deka et al. disclose a reagent for identifying, counting, and classifying blood cells using flow cytometry. The reagent comprises a lysing agent or non-ionic detergent and a fluorescent dye. The non-ionic detergent may be polyoxyethylene ethers and sorbitans (Tween X) (see column 4, lines 46-59). Stains used with the reagent include Acridine Orange and TO-PRO-3 (see column 6, lines 9-22). According to Deka et al., cell fixation is used to transport or penetrate fluorescent stain into cells through cell membrane to stain RNA (see column 5, line 14 to column 10, line 4). Deka et al. teach using formaldehyde as fixing agent; hence, a cell penetration agent (see column 5, lines 53-66). The reagent further includes buffer and fixatives (see column 5, lines 12-19).

Response to Arguments

5. Applicant's arguments filed March 22, 2005 have been fully considered but they are not persuasive.

A) Applicant argues that Sakata does not disclose or suggest the claimed invention because the reagent of Sakata comprising a surfactant and a labeling substance are different from and do not function in the same way as in the claimed invention.

In response, claims 1-11 and 19 are anticipated by Sakata because Sakata specifically teaches a reagent comprising a cell lysing agent (ionic detergent or nonionic

detergent or quaternary ammonium salts at concentrations that lyse erythrocytes (column 9, lines 65-67)), a stain that marks intracellular nucleic acids in unlysed nucleated cells (thiazole orange, ethidium bromide, propidium iodide etc.), alcohol or gluteraldehyde or paraformaldehyde, and also a buffer or anticoagulant (complexing agent), as recited in the rejected claims. The ionic and nonionic detergents also serve as ionophores of the protonophore type, as recited in the rejected claims.

In as far as the function or intended use, the reagent comprises all the elements of the claimed invention. The recitation of the intended use of the claimed reagent must also result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

B) Applicant argues that Deka does not disclose or suggest the claimed invention, specifically, claims 1-7 and 9-11 invention because Deka is not relevant art as it teaches rapid staining of nucleic acids but is directed to study of non-nucleated cells which are reticulocytes. The instant invention is drawn to identifying and counting nucleated cells upon lysis of red cells.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., [staining of] nucleus in nucleated cells) is not recited in the rejected claims. As the reticulocytes taught by Deka have intracellular nucleic acids and ribonucleic acids (RNA

debris) and are not lysed, the teaching of Deka reads on the claimed invention. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Additionally, claims 1-7, 9-11, and 19 are anticipated by Deka because Deka specifically teaches a reagent comprising a cell lysing agent, a stain that marks intracellular nucleic acids in unlysed RNA cells, formaldehyde, and also a buffer, as recited in the rejected claims. The reagent comprises all the elements of the claimed invention. In as far as the function and intended use, the recitation of the intended use of the claimed reagent must also result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963).

5. No claims are allowed.

6. Applicant's submission of the requirements for the joint research agreement prior art exclusion under 35 U.S.C. 103(c) on March 22, 2005 prompted specfic new grounds of rejection under 37 CFR 1.109(b) presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.02(l)(3). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
May 26, 2005

CHRISTOPHER L. CHIN
PRIMARY EXAMINER
GROUP ~~1800~~ 1641